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REVIEW ARTICLE

Shifting paradigms in hypertrophic cardiomyopathy: the role of exercise in disease management

Lara-Marie Yamagata,[1] Kentaro Yamagata,[1,2] Alexander Borg,[1] Mark Abela[1,3]

ABSTRACT

Hypertrophic cardiomyopathy (HCM) is traditionally associated with exercise restriction due to potential risks, yet recent evidence and guidelines suggest a more permissive stance for low-risk individuals. The aim of this comprehensive review was to examine existing research on the impact of exercise on cardiovascular outcomes, safety, and quality of life in this population and to consider implications for clinical practice. Recent studies suggest that regular exercise and physical activity in low-risk individuals with HCM are associated with positive outcomes in functional capacity, haemodynamic response, and quality of life, with consistent safety. Various studies highlight the safety of moderate-intensity exercise, showing improvements in exercise capacity without adverse cardiac remodelling or significant arrhythmias. Psychological benefits, including reductions in anxiety and depression, have been also reported following structured exercise programmes. These findings support the potential benefits of integrating individualised exercise regimens in the management of low-risk individuals with HCM, with the aim of improving their overall well-being and cardiovascular health. Adoption of the FITT (frequency, intensity, time, and type of exercise) principle, consideration of individual risk profiles, and shared decision-making are recommended. Future research is warranted to clarify the definition of 'low risk' for exercise participation and investigate the influence of physical activity on disease progression in HCM. Innovation in therapeutic strategies and lifestyle interventions, alongside improved patient and provider education, will help advance the care and safety of individuals with HCM engaging in exercise. (Hellenic Journal of Cardiology 2024;80:83-95)

1. INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is a multifaceted cardiovascular disorder characterised by abnormal thickening of the heart muscle, primarily affecting the left ventricle (LV), often in combination with microvascular dysfunction and myocardial scar. It is the most common inherited cardiac condition, with a prevalence ranging from one in 200-500 individuals.[1,2] HCM can have a significant impact on cardiac structure and function, leading to various clinical manifestations, symptoms, and potential complications, including atrial fibrillation (AF), stroke, progressive or advanced heart failure (HF), ventricular arrhythmias, and sudden cardiac death (SCD).[2,3]

The management of HCM traditionally focused on pharmacological and invasive interventions to alleviate symptoms and reduce the risk of adverse outcomes.[2] However, recent data are increasingly demonstrating the potential benefits of lifestyle modification. While exercise has been recognised as

[1]Department of Cardiology, Mater Dei Hospital, Msida, Malta
[2]Institute of Sport, Manchester Metropolitan University, Manchester, United Kingdom
[3]Cardiovascular and Genomics Research Institute at St George's, University of London, London, United Kingdom
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an established therapeutic modality in various cardiovascular conditions, its role in the management of HCM has been a subject of debate due to concerns about the potential risks of exercise in this population.[4] Historically, HCM was regarded as a cause of SCD in athletes, which led to conservative exercise recommendations,[5,6] inadvertently promoting a sedentary lifestyle, leading to obesity and increased cardiovascular risk.[4] In contrast, recent evidence indicates that exercise might have a positive effect on cardiovascular remodelling in low-risk HCM patients. In fact, moderate-intensity exercise has been found to pose no significant safety concerns.[7-10] As outlined in the 2019 American College of Cardiology/American Heart Association (ACC/AHA) guidelines, exercise intensity is classified according to metabolic equivalents (METs), with moderate-intensity exercise ranging from 3 to 5.9 METs. This includes activities such as brisk walking at 2.4 to 4 miles per hour, biking at 5 to 9 miles per hour, recreational swimming, and active yoga.[11]

The challenge of exercise restriction in HCM is addressed in various guidelines with differing recommendations (**Table 1**). The 2020 ACC/AHA guidelines recommend low-to-moderate-intensity recreational exercise but underline the importance of annual comprehensive risk evaluation for athletes with HCM participating in more strenuous activities, including competitive sports.[13] Conversely, the European Society of Cardiology (ESC) has adopted a more permissive approach, advising that high-intensity and competitive sports be considered in low-risk individuals with HCM (Class IIB, Level B).[12]

This comprehensive literature review aims to evaluate the existing evidence concerning exercise in HCM and provide recommendations for clinical practice.

2. PATHOPHYSIOLOGY, CLINICAL FEATURES, AND INVESTIGATION OF HCM

The underlying mechanisms of HCM involve a combination of genetic factors causing cellular and molecular abnormalities that consequently lead to structural and functional changes in the heart.[14] Mutations in genes encoding sarcomere proteins, including myosin heavy chain 7 (*MYH7*) and myosin-binding protein C3 (*MYBPC3*), have been identified in 40%-60% of patients with HCM.[15] These mutations result in abnormal sarcomere function, impaired calcium handling, and altered signalling pathways, leading to cellular and molecular mechanisms contributing to hypertrophy, endothelial dysfunction, and myocardial fibrosis.[16]

Histological changes in HCM include myocardial fibrosis, myocyte disarray, and small vessel

TABLE 1 Exercise recommendations for patients with hypertrophic cardiomyopathy

2023 ESC guidelines[12]		2020 AHA/ACC guidelines[13]	
Recommendations	**Class (level)**	**Recommendations**	**Class (level)**
Regular low- to moderate-intensity exercise is recommended in otherwise healthy individuals.	I (C)	Mild- to moderate-intensity recreational exercise is suggested for most individuals with HCM, aligned with the general population's physical activity recommendations.	1 (B-NR)
Individualised risk evaluation recommended for all cardiomyopathy patients when prescribing exercise regimens.	I (C)	It is recommended that athletes with HCM undergo thorough assessments and discuss with expert providers about the potential risks associated with sports involvement.	1 (C-EO)
In genotype-positive phenotype-negative individuals, high-intensity exercise and competitive sports may be considered.	IIa (C)	For most patients with HCM, participation in low-intensity competitive sports is reasonable.	2a (C-EO)
High-intensity physical activities and competitive sports can be considered for asymptomatic, low-risk mild morphological HCM without resting or inducible LVOTO or exercise-induced complex ventricular arrhythmias.	IIb (B)	In genotype-positive phenotype-negative individuals, competitive athletics of any intensity is reasonable.	2a (C-LD)
Avoid high-intensity exercise and sports in high-risk individuals, especially with LVOTO and exercise-induced arrhythmias.	III (C)	Participation in high-intensity recreational activities or moderate- to high-intensity competitive sports may be considered after yearly comprehensive evaluation and shared discussion with an expert provider, with clear communication about SCD and ICD risks.	2b (C-LD)
		ICD implantation solely for competitive sports participation is not recommended.	3: Harm (B-NR)

AHA/ACC = American Heart Association/American College of Cardiology; ESC = European Society of Cardiology; HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter defibrillator; LVOTO = left ventricular outflow tract obstruction; QoL = quality of life; SCD = sudden cardiac death. Adapted from Arbelo et al. (2023)[12] and Ommen et al. (2020).[13]

abnormalities, which may be related to specific genotypes.[17,18] From a clinical perspective, HCM features increased left ventricular thickness, diastolic dysfunction, and dynamic left ventricular outflow tract obstruction (LVOTO), leading to symptoms such as dyspnoea, chest pain, and syncope.[19]

The clinical manifestation of HCM is complex, with variable onset of symptoms, rate of disease progression, and prognosis. The severity of LV hypertrophy and the presence of certain genetic mutations can influence the phenotypic expression of HCM.[18] Electrophysiological abnormalities, such as ventricular arrhythmias and AF, are common in HCM patients, affecting 20%-30% and 25%, respectively, and can further contribute to disease progression.[16,20] Exercise intolerance is a frequent manifestation in HCM as a result of diastolic dysfunction, abnormal myocardial relaxation, microvascular dysfunction, and dynamic LVOTO.[21,22] Reduced exercise capacity is an important predictor of adverse cardiovascular events in HCM associated with more severe symptoms, hospitalisation (arrhythmias/HF), implantable cardioverter-defibrillator (ICD) implantation, and all-cause mortality.[23,24]

Various investigations help evaluate disease severity and progression, including electrocardiography (ECG), laboratory testing, genetic testing, ambulatory ECG monitoring, and cardiac imaging modalities.[12] Echocardiography allows for the assessment of LV wall thickness, LVOTO, and systolic anterior motion of the mitral valve. It also provides information on systolic and diastolic function, global longitudinal strain, left atrial size, and other structural and valvular abnormalities.[13] Cardiac magnetic resonance (CMR) provides detailed information on myocardial morphology and tissue characterisation, including the assessment of myocardial fibrosis and ischaemia. In addition, exercise stress echocardiography can detect dynamic LVOTO and correlate it with exercise-induced symptoms.[12,25] The ESC and AHA guidelines both recommend exercise stress echocardiography for symptomatic patients, attempting to unmask a high left ventricular outflow tract (LVOT) gradient of >50 mm Hg and exercise-induced mitral regurgitation.[12,13]

Exercise testing plays a key role in risk stratification by evaluating arrhythmic burden during exercise, haemodynamic response, and functional capacity. Non-sustained ventricular tachycardia (NSVT) and an abnormal blood pressure (BP) response during exercise are well established risk factors for SCD per the ESC guidelines.[12] Cardiopulmonary exercise testing (CPET) can provide a clear picture of functional capacity, haemodynamic response, and exercise-induced arrhythmias.[26] The latest American and European cardiomyopathy guidelines recommend serial CPET every 2-3 years to objectively monitor functional capacity.[12,13]

3. OUTCOMES AND LONG-TERM EFFECTS OF EXERCISE IN PATIENTS WITH HCM

Several studies on the impact of exercise on cardiovascular outcomes and long-term effects in patients with HCM have been conducted (Table 2). Various end points have been examined, including functional capacity, haemodynamic response, safety and adverse events, quality of life (QoL), and mental health. Notably, most patients recruited in these studies were 'low-risk' individuals,[28,33] and those who did not adhere to recommended clinical follow-ups or led a sedentary lifestyle were often excluded.[32] High-risk patients with HCM, including those with New York Heart Association (NYHA) Class III/IV symptoms, a history of exercise-induced syncope or arrhythmias, LVOTO, and other conditions in which exercise was contraindicated, were also often excluded.[7,8,27,29,30]

3.1. IMPACT OF EXERCISE ON FUNCTIONAL CAPACITY AND HAEMODYNAMIC RESPONSE. The impact of exercise on functional capacity and haemodynamic response in patients with HCM has been the focus of various studies, most of which demonstrated a positive response after engaging in an exercise programme (Table 2 and Fig. 1).

In the RESET-HCM trial, 16 weeks of moderate-intensity aerobic training led to a small but statistically significant increase in exercise capacity compared with usual activity ($p = 0.02$), without significant differences in measures of cardiac morphology and function, LVOT gradient, or serum brain natriuretic peptide (BNP) levels.[8] Dejgaard et al. (2018) found that lifetime vigorous exercise correlated with larger LV end-diastolic volume in both phenotype-positive (HCM left ventricular hypertrophy [LVH]+) and genotype-positive phenotype-negative (G + LVH−) individuals (both $p < 0.001$). Lifetime vigorous exercise also correlated with increased LV mass in G + LVH− individuals ($p = 0.03$) but not in HCM LVH + patients ($p = 0.53$).[30] Using the same study cohort, Andreassen et al. (2022) showed that exercise training during childhood and adolescence was associated with favourable LV diastolic function in those with HCM LVH+ and G + LVH−.[29] In contrast, in another study by Pelliccia et al. (2022), continued sport participation in adult patients with HCM did not result in changes in LV wall thickness or cavity size, and detraining did not lead to regression of LVH.[28] These findings also suggested that

TABLE 2 Summary of published studies evaluating the effects of exercise in patients with hypertrophic cardiomyopathy

Author, year, study design	Study population and intervention	Functional capacity and haemodynamic response	Safety/adverse events	Quality of life and mental health
Lampert, 2023 (LIVE-HCM)[27] Prospective cohort	N = 1660 participants (8-60 years) with HCM or G + LVH− without conditions precluding exercise. (n = 252 sedentary; n = 709 moderate exercise, n = 699 vigorous exercise [including 259 competitive athletes]) Mean ± SD age: 39 ± 15 years; 60% male.		Death/SCA/ICD therapy/arrhythmic syncope: 4.6% overall. By group: non-vigorous exercise: 4.6%; vigorous exercise: 4.7%. Rates of events were not higher in the vigorous exercise group compared with moderate or sedentary groups. SCA/SCD incidents (all male): Vigorous exercise group: n = 7 (3 SCAs during exercise, 2 SCDs, 1 SCA in daily activities, 1 unknown; 1 had ICD). Moderate exercise group: n = 4 (1 SCA during exercise, 3 SCDs; 1 had ICD). Sedentary group: n = 3 (2 SCDs during sleep, 1 SCA while standing; 1 had ICD).	
Pelliccia, 2022[28] Retrospective	N = 60 patients with HCM in competitive sports at time of first diagnosis; 85% were low-risk. Mean ± SD age: 31 ± 16 years; 92% male Final evaluation after 7.0 ± 4.7 years of follow-up, with n = 43 (72%) HCM-detrained and n = 17 (28%) HCM-trained.	77% had LV end-diastolic dimension of 45-54 mm. Normal LV filling in 85%; abnormal septal e' velocities (≤8 cm/s) in n = 20, high E/e' ratios (>14) in n = 12 on tissue Doppler imaging. Enlarged left atrial size in 55% (≥40 mm). No differences in LV size/thickness by sport participation. Mild increase in left atrium size over time; no changes in LV filling parameters. T-wave inversion prevalence decreased in detrained from 86% to 60% and in trained from 94% to 47% ($p < 0.05$). Atrial enlargement increased mostly in trained group (0%-24%, p = 0.024).		
Andreassen[a], 2022[29] Cross-sectional, retrospective	N = 187 participants with HCM LVH+ (n = 121) and genotype-positive family members with no significant LVH (defined as G + LVH−, n = 66). Mean ± SD age: 49 ± 16 years; 52.4% male.	Childhood/adolescent exercise linked to better LV diastolic function in both HCM LVH+ and G + LVH− groups. No negative correlation found between diastolic parameters and exercise exposure.		
Dejgaard[a], 2018[30] Cross-sectional, retrospective		In G + LVH− and HCM LVH + participants: lifetime vigorous exercise increased LV end-diastolic volume ($p < 0.001$). In G + LVH− only: increase in LV mass with lifetime vigorous exercise (p = 0.03). LV systolic function similar between athletes and non-athletes; HCM LVH + athletes had lower E/e' (p = 0.03) and higher e' (p = 0.02) than non-athletes.	In HCM LVH + participants, lifetime vigorous exercise was similar between those with and without ventricular arrhythmias (p = 0.89).	
Basu, 2021[31] RCT	N = 80 young patients with HCM; 12-week HIT programme (n = 40) vs. usual care (n = 40). Mean ± SD age: 45.7 ± 8.6 years.	At 12 weeks: Increase in VO_2peak, VO_2/kg at AT, time to AT, max ET; decrease in systolic BP, BMI (all $p < 0.01$) in exercise group vs. usual care. At 6 months: Maintenance of some exercise gains in time to AT, max ET, VO_2/kg at AT (all $p < 0.05$).	At 12 weeks: No significant differences in arrhythmia safety, NSVT, and ectopic burden (all $p > 0.5$). No sustained episodes of arrhythmias; stable NSVT incidence over time (p = 0.09).	At 12 weeks: Decrease in anxiety ($p \leq 0.001$) and depression scores (p = 0.015) in exercise group vs. usual care. At 6 months: Continued decrease in anxiety ($p < 0.001$); 33/34 maintained exercise adherence.
Kwon, 2021[32] Observational	N = 7666 individuals with HCM who underwent health check-ups, including PA level questionnaires. To estimate individual PA levels, the PAS was calculated, and the study population was categorised into 3 groups according to tertiles of PAS. Mean follow-up of		Decrease in all-cause and CV mortality from lowest to highest PA tertiles: Lowest PA (mean PAS 1.4 ± 0.6 METs/day): 9.1% all-cause, 4.7% CV; Middle PA (mean PAS 3.4 ± 0.7 METs/day): 8.9% all-cause, 3.8% CV; Highest PA (mean PAS 8.4 ± 3.1 METs/day): 6.4% all-cause, 2.7%	

Continued on the next page

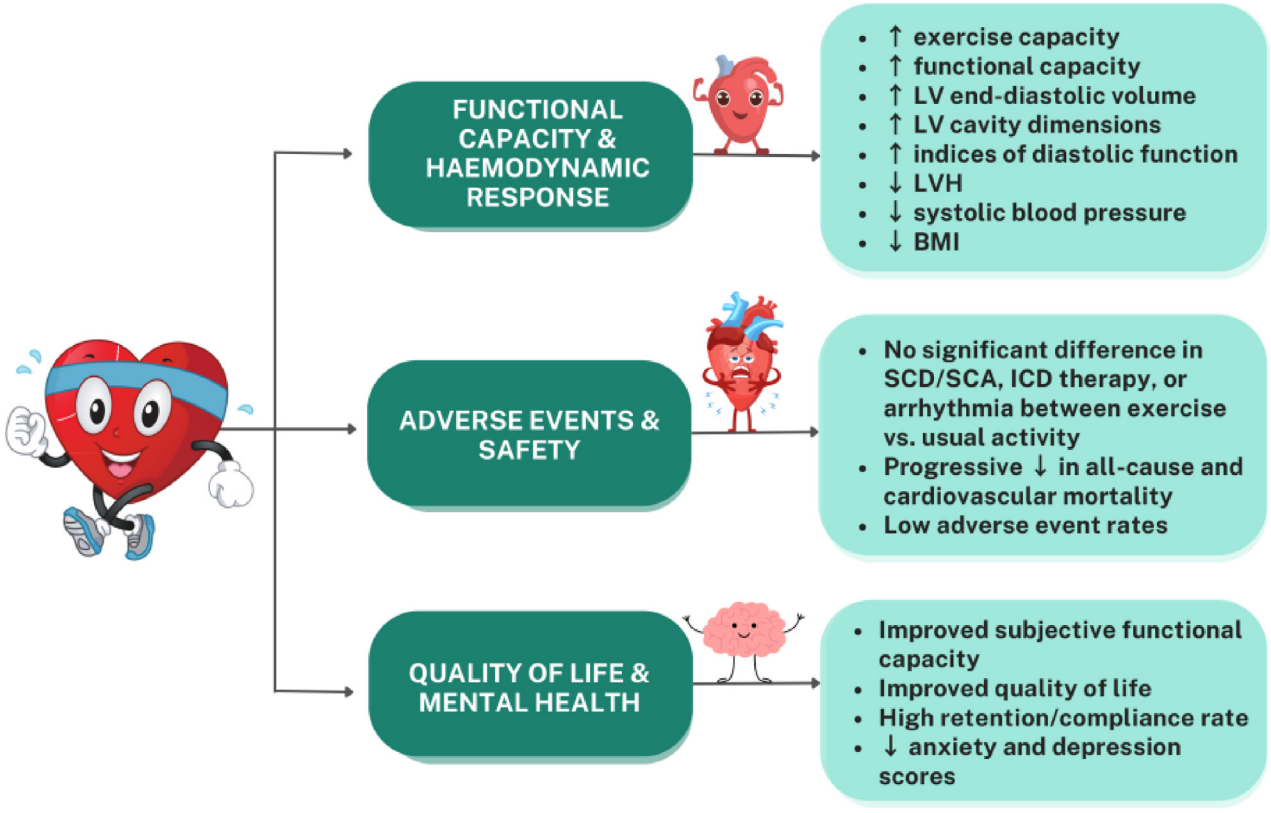
TABLE 2 Continued

Author, year, study design	Study population and intervention	Functional capacity and haemodynamic response	Safety/adverse events	Quality of life and mental health
	5.3 ± 2.0 years. Mean age: 59.5 years; 70.1% male.		CV. p-for-trend = 0.0144 (all-cause), 0.0023 (CV). No increased mortality risk in highest vs. middle PA group (HR 0.78 [95% CI 0.63-0.95] all-cause, HR 0.75 [95% CI 0.54-1.03] CV).	
Pelliccia, 2020[33] Retrospective	N = 88 athletes with HCM in long-term exercise programmes and competitive sports; 88% were low-risk. Median (IQR) age: 31 (19-44) years; 92% male Evaluation after 7 ± 5 (1-21) years, when n = 61 (69%) had reduced/stopped exercise and sport (HCM-detrained), and n = 27 (31%) continued with regular training and sport competitions (HCM-trained).	All athletes had normal systolic LV function; 81% had normal LV filling. Abnormal e' velocity observed in 52% (n = 12/23) of a subset of athletes assessed by tissue Doppler imaging. Enlarged left atrial size was found in 56% (transverse diameter ≥40 mm).	SCA/death rate: 0.3% per year (n = 2; both events off-sport). 22% reported symptoms: syncope (n = 3), palpitations (n = 10), chest pain (n = 4), dyspnoea (n = 2). No difference in SCA/death or symptoms between HCM-trained vs. detrained (Kaplan-Meier p = 0.264).	
Wasserstrum, 2019[34] Observational	N = 45 patients with HCM (>18 years) who participated in a cardiac rehabilitation programme for at least 3 consecutive months. Mean ± SD age (at diagnosis): 49 ± 18 years; mean ± SD age (on admission): 58 ± 13 years; 69% male.	Increase in exercise capacity: from 5.3 to 6.7 METs (p = 0.01) at higher peak heart rates. 56% improved in exercise capacity without changes in NYHA class, clinical, ECG, or echocardiography parameters. Benefit of exercise was more pronounced with <6.8 METs at baseline (p = 0.008).	No significant arrhythmias or events; 1 non-lethal NSVT during exercise.	40% reported an improved subjective perception of functional capacity and QoL. 9% discontinued participation because of discomfort.
Saberi, 2017[8] (RESET-HCM) RCT	N = 136 adults with HCM; 16-week moderate-intensity aerobic training (n = 67) vs. usual activity (n = 69). Mean ± SD age: 50.4 ± 13.3 years; 58% male.	Increase in mean peak VO_2 at 16 weeks in exercise group: 1.27 (95% CI 0.17-2.37, p = 0.02). No significant changes in cardiac morphology/function, LVOT gradient, or serum BNP.	No ventricular arrhythmia, SCA, ICD shocks, or deaths in either group.	SF-36v2 physical functioning scale: +5.7 in exercise group, −2.5 in usual-activity group (difference +8.2, 95% CI 2.6-13.7 points).
Klempfner, 2015[7] Prospective, non-randomised	N = 20 patients with symptomatic HCM, limited in everyday activity, who exercised in a cardiac rehabilitation centre twice a week. Mean ± SD age: 62 ± 13 years; 70% male.	Improvement in functional capacity from 4.7 ± 2.2 to 7.2 ± 2.8 METs (p = 0.01); 50% showed ≥1 grade of improvement in NYHA class with no deterioration during follow-up.	No adverse events or sustained ventricular arrhythmias occurred during training.	
Sheikh, 2015[9] Observational	N = 106 athletes with HCM competing at regional, national, or international levels in a range of sports. Mean ± SD age: 24.3 ± 6.9 years; 94.3% male N = 101 sedentary patients with HCM Mean ± SD age: 25.8 ± 6.0 years; 90.1% male A subset of athletes (n = 15) with HCM exhibiting morphologically mild, concentric disease was compared with 55 healthy athletes with mild physiological LVH.	Athletes: 96% had T-wave inversion, milder LVH, larger LV cavity size, and better overall diastolic function vs. sedentary group (p < 0.001). Average E/E' ratio was smaller in athletes vs. sedentary group (p < 0.001).	Athletes: 13.2% had exercise test abnormalities; 8.5% had blunted BP response (systolic rise of <25 mm Hg), vs. 22.8% in sedentary group (p = 0.004). 5.6% had exercise-induced arrhythmias, including NSVT, SVT, AF, and ventricular ectopics. On 24-hr Holter, 12.3% had arrhythmias; 9.4% had non-specific findings including couplets and triplets, frequent ventricular ectopics, and a junctional rhythm. Athletes with mild concentric HCM: No exercise test abnormalities; 6.7% (n = 1) had NSVT on 24-hr Holter. Healthy athletes with physiological LVH: No abnormalities in exercise testing or Holter.	

AF = atrial fibrillation; AT = anaerobic threshold; BMI = body mass index; BNP = b-type natriuretic peptide; BP = blood pressure; CI = confidence interval; CV = cardiovascular; ET = exercise time; G + LVH− = genotype-positive phenotype-negative; HCM = hypertrophic cardiomyopathy; HCM LVH+ = phenotype-positive; HIT = high-intensity training; HR = hazard ratio; ICD = implantable cardioverter defibrillator; IQR = interquartile range; LV = left ventricular; LVH = left ventricular hypertrophy; LVOT = left ventricular outflow tract; MET = metabolic equivalent of task; NSVT = non-sustained ventricular tachycardia; NYHA = New York Heart Association; PA = physical activity; PAS = physical activity score; QoL = quality of life; RCT = randomised controlled trial; SCA = sudden cardiac arrest; SCD = sudden cardiac death; SD = standard deviation; SF-36v2 = 36-item Short-Form Health Survey; SVT = sustained ventricular tachycardia; VO_2/kg at AT = oxygen consumption/kg at anaerobic threshold; VO_2peak = peak oxygen consumption. [a]Andreassen et al.[29] and Dejgaard et al.[30] assessed the same study cohort but examined different outcomes.

detraining could be very useful in differentiating physiological LVH from pathological hypertrophy in HCM. The contrasting results may be attributed to the different patient populations studied (the latter study included athletes, whilst the former examined the effect of exercise in early life). Sheikh et al. (2015)

FIGURE 1 **Effects of Exercise in Patients with Hypertrophic Cardiomyopathy**



BMI = body mass index; ICD = implantable cardioverter-defibrillator; LV = left ventricle; LVH = left ventricular hypertrophy; SCA = sudden cardiac arrest; SCD = sudden cardiac death.

examined the effects of exercise on structural parameters and found that athletes with HCM exhibited milder LVH, larger LV cavity dimensions, and superior indices of diastolic function compared with sedentary HCM patients (all $p < 0.001$).[9]

Studies by Basu et al. (2021) and Klempfner et al. (2015) demonstrated that structured training programmes could lead to increased exercise capacity and improved functional capacity.[7,31] In addition, the randomised controlled trial (RCT) by Basu et al. also reported greater reductions in systolic BP ($p = 0.002$) and body mass index (BMI) ($p < 0.001$) in the exercise group who underwent a 12-week high-intensity training programme compared with patients who received usual care. Similarly, in a study by Wasserstrum et al. (2019), participation in a cardiac rehabilitation programme for at least 3 months was associated with a significant increase in exercise capacity ($p = 0.01$) at higher peak heart rates; this benefit was particularly pronounced in patients with lower exercise capacity at baseline ($p = 0.008$).[34]

3.2. IMPACT OF EXERCISE ON ADVERSE EVENTS AND SAFETY OUTCOMES. Across several studies, the evaluation of safety-related adverse outcomes in exercise interventions among low-risk individuals with HCM demonstrated a generally consistent pattern (Table 2 and Fig. 1).

In the LIVE-HCM study, the primary composite end point of death, sudden cardiac arrest (SCA), and appropriate ICD therapy or arrhythmic syncope was reached by 4.6% of participants, with no significant difference between vigorous and non-vigorous exercise groups.[27] Basu et al. (2021) reported no significant differences between groups (12-week high-intensity training programme vs. usual care) in composite arrhythmia safety outcomes at 12 weeks.[31] Similarly, in the RESET-HCM trial, there were no occurrences of sustained ventricular arrhythmia, SCA, appropriate ICD shock, or death in either group (exercise vs. usual

activity).[8] Dejgaard et al. (2018) found that the performance of lifetime vigorous exercise was similar between individuals with HCM LVH+ with and without ventricular arrhythmias ($p = 0.89$).[30]

In the study by Kwon et al. (2021), moderate-to-vigorous-intensity physical activity in middle-aged patients with HCM was associated with a progressive reduction of all-cause and cardiovascular mortality.[32] Klempfner et al. (2015) and Wasserstrum et al. (2019) reported no adverse events or significant arrhythmias throughout participation in their respective training programmes.[7,34] Furthermore, in the study by Sheikh et al. (2015), none of the 15 athletes with mild concentric HCM revealed abnormalities on exercise testing, and only one demonstrated arrhythmia (NSVT) on 24-h Holter monitoring.[9] Pelliccia et al. (2020) also reported low adverse event rates, with two instances of SCA or death (0.3% per year), both of which occurred outside of sport participation, and no significant differences in Kaplan-Meier analyses of freedom from SCA/SCD and symptoms between HCM-trained and detrained patients.[33] These findings indicate that exercise may be conducted without significant increases in risk for serious arrhythmias or other adverse events in low-risk individuals with HCM.

3.3. IMPACT OF EXERCISE ON QUALITY OF LIFE AND MENTAL HEALTH OUTCOMES. In terms of patient-reported outcomes, including QoL and psychological measures, studies examining the effects of exercise in patients with HCM demonstrated enhanced physical functioning and highlighted the potential therapeutic role of exercise in reducing anxiety and depression (Table 2 and Fig. 1).

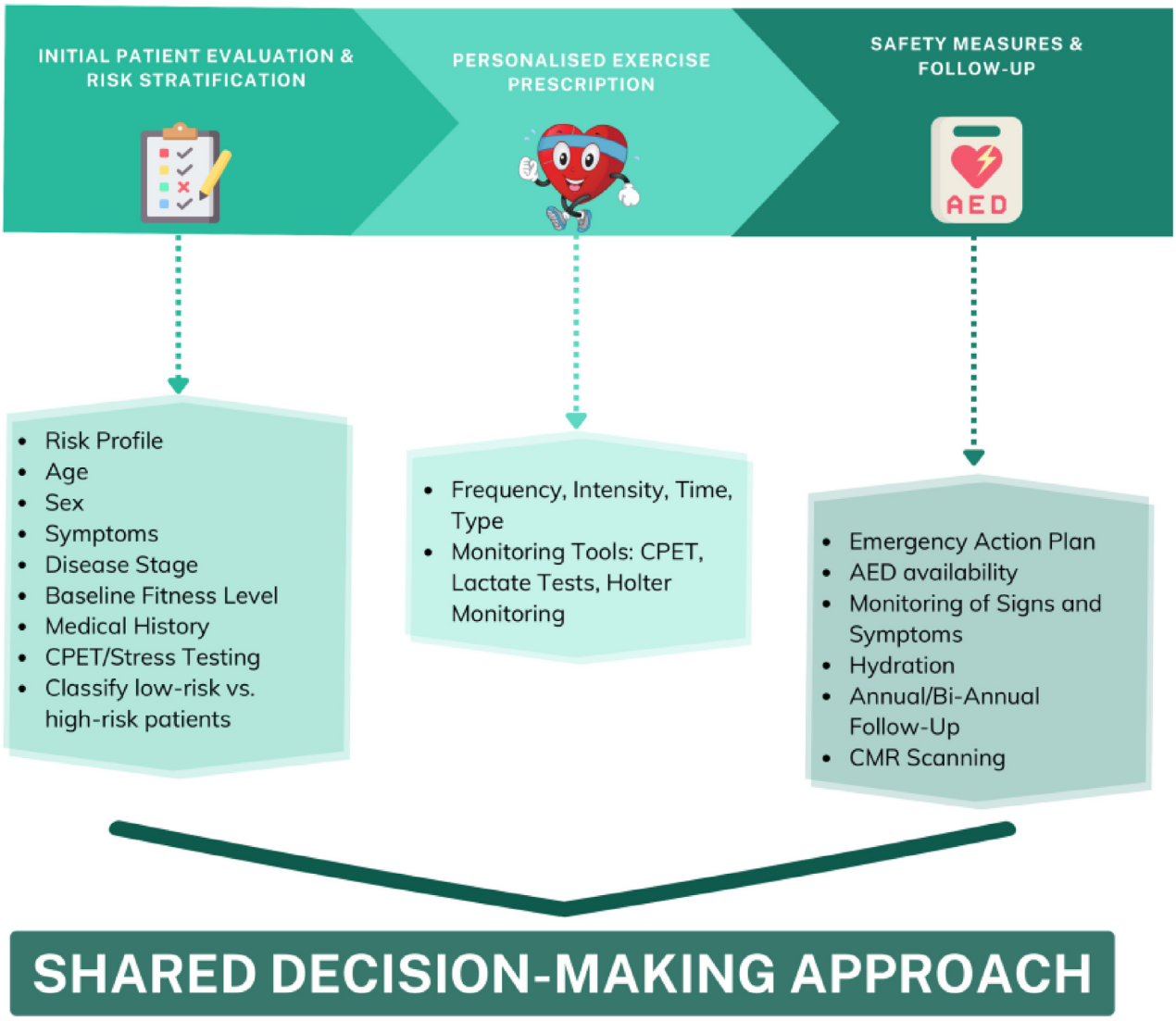
In the RESET-HCM trial, a significant difference was observed in the 36-item Short-Form Health Survey (SF-36v2) physical functioning scale, where the exercise group experienced an increase of 5.7 points, as opposed to a decrease of 2.5 points in the usual-activity group.[8] Additionally, Wasserstrum et al. (2019) reported that training improved the subjective perception of functional capacity and QoL in approximately 40% of participants.[34] Notably, the retention rate in the training programme was high, with only four patients (9%) discontinuing because of discomfort. Basu et al. (2021) revealed a positive effect of exercise on mental health; at 12 weeks, the exercise group had a greater reduction in anxiety ($p \leq 0.001$) and depression ($p = 0.015$) scores, with the reduction in anxiety continuing at the 6-month follow-up ($p < 0.001$).[31] Additionally, patient-reported exercise adherence at 6 months was comparable to baseline physical activity in most individuals from the exercise group who attended follow-up.[31] These findings highlight the positive effects of exercise interventions on both the physical and psychological aspects and QoL of patients with HCM. Moreover, the high adherence and retention rates suggest that, with careful monitoring and tailoring to individual needs and preferences, a structured exercise programme may be a well-tolerated component of care for individuals with HCM.

4. EXERCISE PRESCRIPTION IN HCM

As discussed, exercise in HCM, including vigorous regimens, provides consistent physical and psychosocial benefits. This is also supported by pre-clinical models.[10] Collectively, these findings support integrating personalised and closely monitored exercise programmes into the therapeutic approach for HCM patients, without forgetting the importance of a shared decision-making model to balance patient needs with potential risks. Translating these promising research findings into clinical practice requires meticulous consideration and individualisation. Although the general trend demonstrates the safety and efficacy of exercise in HCM, the potential complexity of HCM entails that a one-size-fits-all approach is inadequate, and it is necessary to consider specific symptoms, fitness levels, risk profiles, and patient preferences. A summary of a proposed individualised approach to exercise prescription in patients with HCM is presented in Fig. 2.

4.1. INDIVIDUALISED EVALUATION AND EXERCISE PRESCRIPTION. 4.1.1. Baseline assessments. Before initiating an exercise prescription in individuals with HCM, a thorough evaluation to determine the risk of SCA should be conducted, considering the individual's risk profile, age, sex, symptoms, disease stage, baseline fitness and previous training experience, and medical history.[4,13,26,35,36] As described previously, initial investigations may include ECG, Holter monitoring, laboratory investigations, and multi-modality imaging. CPET allows for a detailed assessment of functional capacity and mechanisms of exercise intolerance. It also enables stratification through evaluation of parameters such as peak oxygen consumption ($PeakVO_2$), ventilatory anaerobic threshold (VAT), ventilatory efficiency, and arrhythmia and BP response to exercise.[37] Stress echocardiography may be used to rule out dynamic LVOTO in those reporting chest pain or syncope during exercise.[38] Additionally, ambulatory tools such as Holter monitoring or wearables during exercise could be considered, thereby

FIGURE 2 **Individualised Approach to Exercise Prescription in Patients with Hypertrophic Cardiomyopathy**



AED = automated external defibrillator; CMR = cardiac magnetic resonance; CPET = cardiopulmonary exercise testing.

enhancing risk stratification models by detecting exercise-induced arrhythmias.[35]

4.1.2. The FITT principle and recommendations for individuals with HCM. Exercise prescriptions should be guided by the FITT (frequency, intensity, time, and type of exercise) principle.[39] Guidelines strongly advise implementing a shared decision-making approach, striving towards establishing a compromise between cardiovascular benefit, patient values, and individual objectives.[13] An example of the FITT principle tailored for individuals with HCM is provided in Table 3.

The general recommendations for moderate-intensity physical activity among adults typically include 150-300 min of aerobic activities weekly, preferably spread throughout the week, with a potential gradual increase in frequency and/or intensity unless contraindicated.[40,42] Exercise prescription should be led by specialists trained in inherited cardiac conditions who are well accustomed to exercise prescription. Mild-to moderate-intensity recreational exercise is safe for most individuals with HCM.[12,13] Disease severity, risk profile, and functional capacity achieved during exercise testing will help guide the

TABLE 3 Example of the FITT principle tailored for individuals with HCM

FITT Component	Description
Frequency	Preferably spread throughout the week (eg, 30 min a day, 5 days a week).[40]
Intensity	• Low-intensity: 1.6-2.9 METs; target HRmax <55%; Borg RPE Scale 6-11. • Moderate-intensity: 3.0-5.9 METs; target HRmax 55%-74%; Borg RPE Scale 12-14.[11,12,41]
Time (Duration)	150-300 min of moderate-intensity aerobic physical activity.[42]
Type of exercise[a]	• Low-intensity: light housework, slow walking. • Moderate-intensity: activities such as brisk walking at 2.4 to 4 miles per hour, biking at 5 to 9 miles per hour, recreational swimming, and active yoga.[11]

HRmax = maximum heart rate; MET = metabolic equivalent; RPE = rate of perceived exertion. [a]There are insufficient data regarding recommendations for strength exercise.[13]

level of exercise intensity. Depending on the outcome of this evaluation, patients are then encouraged to engage in exercise according to their individualised exercise prescription. Peak METs during stress testing will help determine appropriate activities. Heart rate and the Borg scale (<15 for low to moderate intensity)[41] are practical measures of intensity, easily adopted by patients when engaging in an exercise routine. Activities achieved with <3 METs and/or <55% target maximum heart rate (HRmax) are classified as low-intensity (eg, slow walking and light housework). Moderate-intensity exercise routines include activities achieved with 3.0-5.9 METS (55%-74% of HRmax), such as recreational swimming, brisk walking, and yoga.[11]

Strength training may also be carefully and gradually incorporated, with a focus on not exceeding 70% HRmax,[43] particularly to avoid the range within repetitions that could provoke the Valsalva manoeuvre. The recommended repetition range is 8-15, avoiding breath-holding or reaching failure (ie, performing exercise until a repetition can no longer be completed because of muscle fatigue).[44] It is also advisable to start with low weights (≤20% of body weight for upper limbs and ≤50% for lower limbs).[26,43] However, to date, there are insufficient data to make recommendations on resistance training, although it is advised to avoid the Valsalva manoeuvre, which can worsen LVOTO.[13]

Regular patient reassessment and monitoring through CPET, which may be complemented by lactate threshold testing using ear lobe blood samples, can effectively identify aerobic and anaerobic thresholds at blood lactate concentrations of 2 mmol/L and 4 mmol/L, respectively. Monitoring aerobic and anaerobic capacities can assist cardiologists, exercise physiologists, and fitness coaches to modify training regimens, individualising exercise intensity targets (Fig. 2).[36]

4.1.3. High-risk individuals. Individuals diagnosed with HCM who harbour high-risk markers (symptoms or a history of cardiac arrest or cardiac syncope, moderate range of ESC SCD score [≥4% at 5 years], LVOTO [LVOT gradient >30 mm Hg at rest], abnormal BP response to exercise, and evidence of arrhythmia at rest or on exertion) should not engage in high-intensity exercise or competitive sports (Class III, Level C).[45] These individuals should be risk-stratified, as outlined in previous sections, and medically optimised accordingly, in close liaison with cardiomyopathy/sports cardiology experts. Low-to moderate-intensity exercise regimens may then be pursued and up-titrated according to the clinical response with close monitoring in expert units.[4]

4.1.4. Patients with an ICD. Individuals with HCM implanted with an ICD were historically discouraged from engaging in any form of physical activity. The criteria for eligibility in competitive sports have now become more liberal, with shared decision-making becoming a key component in the management of these patients.[45] There are various considerations that must be discussed when addressing such situations. Sports activity early on after ICD implantation is discouraged because of an increased risk of lead dislocation. In the long term, sporting disciplines dependent on repeated upper extremity movements are also discouraged because of the risk of lead malfunction (eg, swimming, powerlifting). Sporting disciplines associated with chest trauma (eg, baseball, rugby, football) are also discouraged because of an increased risk of generator failure.[46] Some athletes may also experience inappropriate and/or appropriate ICD shocks during exercise. Individualising device programming is often necessary. Altering ventricular tachycardia/ventricular fibrillation detection rates and tracking rates may be required, especially in individuals with a history of inappropriate therapies. Despite concerns in this regard, long-term results of the Multinational ICD Sports Registry have shown that athletes with ICDs who continued to engage in sports did not have serious adverse sequelae during follow-up.[47] Whilst these results are

encouraging, caution should be exercised; an individualised strategy, under expert supervision is paramount. Importantly, ICD implantation for the sole purpose of participating in competitive or high-intensity sports is not recommended (Class 3, Level B).[13]

4.1.5. Competitive sports participation and athletic considerations. The impact of high-intensity exercise and competitive sports on disease progression in HCM has not been well studied. Previously, athletes with HCM were discouraged from continuing competitive sports. However, our understanding of HCM in athletes has evolved over the past decade. In a study of low-risk adult athletes with HCM, voluntary participation in competitive sports was not associated with increased risk of major cardiac events or clinical worsening compared with those who stopped or reduced participation in exercise programmes or competitive sports.[33] A similar study cohort demonstrated no differences in LV cavity size and wall thickness, regardless of patients' sports participation.[28] In another study, competitive young adult athletes with asymptomatic HCM demonstrated physiological cardiac adaptations similar to those of athletes without HCM.[9]

Participation in competitive sports should be individualised by considering factors such as the athlete's desired sports regimen, preferences, and phenotype.[35] Elite athletes with HCM should seek expert advice to help determine the overall cardiovascular risk, institute appropriate lifestyle and medical therapy, and refer for advanced therapies (devices/surgery) if indicated. Following this comprehensive evaluation, a personalised exercise prescription will aim to strike a balance between benefits and risks. Annual re-evaluations are also warranted to monitor for symptoms and evidence of disease progression.[13,26] Emergency action plans (EAPs), including ensuring access to or purchasing automated external defibrillators (AEDs) and potential medication use, should also be discussed.[26]

Current European guidelines are now more lenient, relying on risk markers and emphasising that shared decision-making is paramount. Participation in high-intensity exercise and competitive sports may be considered in asymptomatic, low-risk individuals with mild morphological manifestations of HCM in the absence of both resting and inducible LVOTO and exercise-induced complex ventricular arrhythmias (Class IIb, Level B). Conversely, engagement in high-intensity exercise and competitive sports should be avoided in high-risk individuals and in those presenting with LVOTO and exercise-induced complex ventricular arrhythmias (Class III, Level C).[12] Individuals meeting the criteria for competitive sports, as outlined by the Sport Cardiology Section of the European Association of Preventive Cardiology (EAPC) guidelines, must adhere to the guidance provided by the EAPC recommendations, presented in Table 4.[48]

4.2. LIFESTYLE ADVICE AND EMERGENCY ACTION PLANS. An EAP should be incorporated in exercise prescriptions, providing guidance on what to do in case of cardiac events during exercise. Preferably, an AED should be readily accessible in exercise venues, including gyms and schools.[26]

Patient education about the importance of hydration, especially in hot environments, is essential to prevent adverse effects on preload and electrolyte balance. Dehydration can trigger or exacerbate obstructive symptoms and arrhythmias. Education

TABLE 4 Exercise recommendations for athletes with hypertrophic cardiomyopathy according to the sport cardiology section of the european association of preventive cardiology (EAPC)

Recommendations	Class (Level)
Participation in intensive exercise and competitive sports should be individually assessed following complete evaluation. Absolute contraindications for sports participation include: 1. History of SCD/SCA; 2. Symptoms, particularly unpredicted syncope; 3. Exercise-induced ventricular tachycardia; 4. High ESC 5-year risk score; 5. Significant increase in LV outflow gradient (>50 mm Hg); 6. Abnormal blood pressure response to exercise.	IIb (C)
• In adults with mild HCM and low ESC risk score, participation in all competitive sports may be considered, except in sports where syncope could cause harm or death. • Decision after comprehensive evaluation and explanation of disease characteristics, risk factors, and potential outcomes. • Athlete and physician should reach reasonable understanding and agreement. • Annual reviews should be conducted to assess symptoms and changes in risk profile.	IIb (C)

ESC = European Society of Cardiology; HCM = hypertrophic cardiomyopathy; LV = left ventricle; SCA = sudden cardiac arrest; SCD = sudden cardiac death. Adapted from Pelliccia et al., 2019.[48]

should also cover the identification of exercise-triggered signs and symptoms, along with knowing when to stop physical activity and seek medical attention. Furthermore, patients should be asked about stimulant use, including caffeine and prescription medications, as these can increase sympathetic tone and contribute to arrhythmogenic risk.[26]

Adherence to the exercise prescription should be strongly encouraged in those desiring to partake in physical activity. Lack of compliance can negate the positive health effects of physical activity, potentially leading to adverse health outcomes. Therefore, patient education on the importance of compliance and the potential risks of non-adherence has to be reinforced during follow-up to ensure that the intended health benefits are not compromised.

4.3. FOLLOW-UP. The 2020 ESC sports cardiology guidelines recommend yearly follow-up for most patients with HCM engaging in regular exercise.[45] However, biannual assessments may be more appropriate for adolescents and young adults given the evolving nature of their disease phenotype and increased susceptibility to exercise-induced SCD. The primary aim of these follow-up evaluations is to monitor disease progression and refine risk stratification.[45] Furthermore, CMR is advisable for individuals with HCM during follow-up to assess disease progression and assist in risk stratification and therapeutic management (Class IIa, Level C).[12] The emergence of new symptoms should necessitate a temporary cessation of exercise activity and prompt reassessment.[45]

4.4. GENOTYPE-POSITIVE PHENOTYPE-NEGATIVE INDIVIDUALS. There is no evidence to support exercise restriction in asymptomatic genotype-positive phenotype-negative individuals. Participation in competitive sports of any intensity can be considered according to the latest guidelines (Class IIa, Level C).[12,13] Annual assessment of these individuals is strongly advised, specifically monitoring for the development of phenotypic features of HCM.[12] A study by Aengevaeren et al. (2019) demonstrated no relationship between lifelong physical activity and genotype-to-phenotype transition in individuals with HCM genes.[49]

4.5. SHARED DECISION-MAKING APPROACH. A collaborative decision-making approach is an important element for exercise prescription in HCM, as it enhances patient autonomy and informed consent, which are indispensable in medical practice.[4,35] Educational interactions and open communication among patients, family members, athletic trainers, and health care providers ensure safety and adherence to clinical guidelines.[26] However, existing risk stratification algorithms for athletes with heart disease are often derived from sedentary population data and may not apply to athletes with unique physical and metabolic demands. The EAPC recommends a tailored approach considering individual symptoms, risk factors for SCD/SCA, age, and sports specifics, with the athlete being fully aware of their risks and condition.[48]

Implementing an exercise programme for those with HCM should involve health care providers, exercise professionals, and patients working together to facilitate appropriate risk assessment, ongoing monitoring, and regular evaluations. A personalised exercise regimen in HCM accounts for each patient's circumstances and integrates exercise safely into their broader care strategy.

5. FUTURE DIRECTIONS AND RESEARCH GAPS

Research on exercise in HCM presents an array of challenges and opportunities. One pressing concern is defining 'low risk' in the context of exercise participation in this patient population. While the notion of 'return to play' has been previously discussed, there is a need to establish robust, evidence-based definitions for what constitutes low risk in HCM. Similarly, SCD risk among the phenotype-negative gene carriers is still a developing area of study and necessitates further research.[12] A research gap also exists in understanding how exercise might affect the natural progression and disease expression of HCM. Large, adequately powered RCTs are warranted to develop effective and safe exercise recommendations.[12] Understandably, given the slow rate of disease progression and the low overall event rates in HCM patients, RCTs may be particularly challenging.[13] Future research should, therefore, also consider alternative trial designs and use specific patient-reported outcome tools to assess the impact of new therapies rigorously.[13]

While the imperative for more robust data is clear, there are unique challenges in implementing exercise interventions in patients with HCM. One such barrier is the limited awareness among health care providers and patients regarding the potential benefits and risks of exercise in this population. This calls for collective efforts in education and the dissemination of evidence-based information. Accessibility is another issue, particularly in resource-limited

settings. Innovative solutions are needed to facilitate better access to exercise facilities and specialists.

Maintaining long-term exercise adherence is a significant challenge for HCM patients despite initial high motivation. Research into motivational strategies and behavioural interventions is essential to improve long-term adherence. Ensuring patient safety through accurate risk stratification, improved prediction models, and standardised safety protocols for exercise is equally important.

Regarding novel therapeutic strategies, the potential synergistic effects of combining exercise with pharmacological interventions offer a promising avenue for exploration. Advances in digital health technology, including wearables and telemedicine platforms, can revolutionise the implementation and monitoring of exercise interventions in HCM. Furthermore, research into novel exercise modalities, such as supervised home-based programmes, could provide more convenient alternatives to traditional, facility-based interventions. Finally, multi-domain lifestyle interventions that combine exercise with other lifestyle changes, such as diet, stress management, and sleep optimisation, should be considered to present a holistic approach to improving cardiovascular outcomes in patients with HCM.

6. CONCLUSION

We have shown evidence supporting the benefits of exercise in low-risk patients with HCM, illustrating improvements in exercise capacity and QoL, and favourable cardiovascular adaptations. In fact, exercise can be considered a complementary modality in the existing management strategies for low-risk patients with HCM. Furthermore, this review highlights the paramount importance of risk stratification, continuous monitoring and follow-up, and adherence to safety protocols in implementing exercise interventions.

Tailoring exercise prescriptions to individual patient characteristics, disease severity, and preferences is another salient point of this review. Individualised interventions using the FITT principle optimise the benefits derived from exercise while minimising associated risks. Importantly, patient education and a shared decision-making approach are fundamental elements for achieving these outcomes. Future research should focus on defining 'low-risk' categories, innovative trial designs, and addressing gaps in long-term adherence, health care provider awareness, and accessibility to optimise the safety and efficacy of exercise interventions in this complex patient population.

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CORRESPONDING AUTHOR. Institute of Sport, Manchester Metropolitan University, Manchester, United Kingdom E-mail: k.yamagata@mmu.ac.uk.

REFERENCES

1. Semsarian C, Ingles J, Maron MS, Maron BJ. New perspectives on the prevalence of hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2015;65(12):1249-1254.

2. Maron B, Desai M, Nishimura R, et al. Diagnosis and evaluation of hypertrophic cardiomyopathy. *J Am Coll Cardiol*. 2022;79(4):372-389.

3. Makavos G, Kairis C, Tselegkidi ME, et al. Hypertrophic cardiomyopathy: an updated review on diagnosis, prognosis, and treatment. *Heart Fail Rev*. 2019;24(4):439-459.

4. Basu J, Malhotra A, Papadakis M. Exercise and hypertrophic cardiomyopathy: two incompatible entities? *Clin Cardiol*. 2020;43(8):889-896.

5. Pelliccia A, Fagard R, Bjørnstad HH, et al. Recommendations for competitive sports participation in athletes with cardiovascular disease: a consensus document from the study group of sports cardiology of the working group of cardiac rehabilitation and exercise physiology and the working group of myocardial and pericardial diseases of the European society of cardiology. *Eur Heart J*. 2005;26(14):1422-1445.

6. Maron BJ, Udelson JE, Bonow RO, et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: task Force 3: hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy and other cardiomyopathies, and myocarditis. *Circulation*. 2015;132(22):e273-e280.

7. Klempfner R, Kamerman T, Schwammenthal E, et al. Efficacy of exercise training in symptomatic patients with hypertrophic cardiomyopathy: results of a structured exercise training program in a cardiac rehabilitation center. *Eur J Prev Cardiol*. 2015;22(1):13-19.

8. Saberi S, Wheeler M, Bragg-Gresham J, et al. Effect of moderate-intensity exercise training on peak oxygen consumption in patients with hypertrophic cardiomyopathy: a randomized clinical trial. *JAMA*. 2017;317(13):1349-1357.

9. Sheikh N, Papadakis M, Schnell F, et al. Clinical profile of athletes with hypertrophic cardiomyopathy. *Circ Cardiovasc Imaging*. 2015;8(7):e003454.

10. Konhilas JP, Watson PA, Maass A, et al. Exercise can prevent and reverse the severity of hypertrophic cardiomyopathy. *Circ Res*. 2006;98(4):540-548.

11. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of cardiology/American heart association task force on clinical practice guidelines. *Circulation*. 2019;140(11):e596-e646.

12. Arbelo E, Protonotarios A, Gimeno JR, et al. 2023 ESC Guidelines for the management of cardiomyopathies: developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC). *Eur Heart J*. 2023;44(37):3503-3626.

13. Ommen SR, Mital S, Burke MA, et al. 2020 AHA/ACC guideline for the diagnosis and

treatment of patients with hypertrophic cardiomyopathy: a report of the American College of cardiology/American heart association joint committee on clinical practice guidelines. *J Am Coll Cardiol*. 2020;76(25):e159–e240.

14. Bos JM, Ommen SR, Ackerman MJ. Genetics of hypertrophic cardiomyopathy: one, two, or more diseases? *Curr Opin Cardiol*. 2007;22(3):193–199.

15. Neubauer S, Kolm P, Ho CY, et al. Distinct subgroups in hypertrophic cardiomyopathy in the NHLBI HCM registry. *J Am Coll Cardiol*. 2019;74(19):2333–2345.

16. Marian AJ, Braunwald E. Hypertrophic cardiomyopathy. *Circ Res*. 2017;121(7):749–770.

17. Noureldin RA, Liu S, Nacif MS, et al. The diagnosis of hypertrophic cardiomyopathy by cardiovascular magnetic resonance. *J Cardiovasc Magn Reson*. 2012;14(1):17.

18. Lipshultz SE, Orav EJ, Wilkinson JD, et al. Risk stratification at diagnosis for children with hypertrophic cardiomyopathy: an analysis of data from the Pediatric Cardiomyopathy Registry. *Lancet*. 2013;382(9908):1889–1897.

19. Varma P, Neema P. Hypertrophic cardiomyopathy: Part 1 - introduction, pathology and pathophysiology. *Ann Card Anaesth*. 2014;17:118–124.

20. Fananapazir L, Tracy CM, Leon MB, et al. Electrophysiologic abnormalities in patients with hypertrophic cardiomyopathy. A consecutive analysis in 155 patients. *Circulation*. 1989;80(5):1259–1268.

21. Matsumoto AY, Arteaga E, Ianni BM, Braga AMFW, Buck PC, Mady C. Relationships among exercise capacity, hypertrophy, and left ventricular diastolic function in nonobstructive hypertrophic cardiomyopathy. *Am Heart J*. 2005;150(1):144–149.

22. Le VV, Perez MV, Wheeler MT, Myers J, Schnittger I, Ashley EA. Mechanisms of exercise intolerance in patients with hypertrophic cardiomyopathy. *Am Heart J*. 2009;158(3):e27–e34.

23. Desai MY, Bhonsale A, Patel P, et al. Exercise echocardiography in asymptomatic HCM: exercise capacity, and not LV outflow tract gradient predicts long-term outcomes. *JACC Cardiovasc Imaging*. 2014;7(1):26–36.

24. Sorajja P, Allison T, Hayes C, Nishimura RA, Lam CSP, Ommen SR. Prognostic utility of metabolic exercise testing in minimally symptomatic patients with obstructive hypertrophic cardiomyopathy. *Am J Cardiol*. 2012;109(10):1494–1498.

25. Shah JS, Esteban MTT, Thaman R, et al. Prevalence of exercise-induced left ventricular outflow tract obstruction in symptomatic patients with non-obstructive hypertrophic cardiomyopathy. *Heart*. 2008;94(10):1288.

26. Bryde R, Martinez MW, Emery MS. Exercise recommendations for patients with hypertrophic cardiomyopathy. *Prog Cardiovasc Dis*. 2023;80:53–59.

27. Lampert R, Ackerman MJ, Marino BS, et al. Vigorous exercise in patients with hypertrophic cardiomyopathy. *JAMA Cardiol*. 2023;8(6):595–605.

28. Pelliccia A, Borrazzo C, Caselli S, et al. Neither athletic training nor detraining affects LV hypertrophy in adult, low-risk patients with HCM. *JACC Cardiovasc Imaging*. 2022;15(1):170–171.

29. Andreassen K, Dejgaard LA, Lie Ø, et al. Exercise training during childhood and adolescence is associated with favorable diastolic function in hypertrophic cardiomyopathy. *Int J Cardiol*. 2022;364:65–71.

30. Dejgaard LA, Haland TF, Lie OH, et al. Vigorous exercise in patients with hypertrophic cardiomyopathy. *Int J Cardiol*. 2018;250:157–163.

31. Basu J, Jayakumar S, Miles C, et al. Six-month outcomes of a high intensity exercise programme in young patients with hypertrophic cardiomyopathy: the SAFE-HCM trial. *Eur J Prev Cardiol*. 2021;28(Supplement_1):zwab061.344.

32. Kwon S, Lee HJ, Han KD, et al. Association of physical activity with all-cause and cardiovascular mortality in 7666 adults with hypertrophic cardiomyopathy (HCM): more physical activity is better. *Br J Sports Med*. 2021;55(18):1034–1040.

33. Pelliccia A, Caselli S, Pelliccia M, et al. Clinical outcomes in adult athletes with hypertrophic cardiomyopathy: a 7-year follow-up study. *Br J Sports Med*. 2020;54(16):1008.

34. Wasserstrum Y, Barbarova I, Lotan D, et al. Efficacy and safety of exercise rehabilitation in patients with hypertrophic cardiomyopathy. *J Cardiol*. 2019;74(5):466–472.

35. Snir WA, Connelly KA, Goodman JM, Dorian D, Dorian P. Exercise in hypertrophic cardiomyopathy: restrict or rethink. *Am J Physiol Heart Circ Physiol*. 2021;320(5):H2101–H2111.

36. Cavigli L, Olivotto I, Fattirolli F, et al. Prescribing, dosing and titrating exercise in patients with hypertrophic cardiomyopathy for prevention of comorbidities: ready for prime time. *Eur J Prev Cardiol*. 2020;28:204748732092865.

37. Mikic L, Ristic A, Markovic Nikolic N, et al. The role of cardiopulmonary exercise testing in hypertrophic cardiomyopathy. 2023. *Medicina (B Aires)*. 2023;59(7):1296. Available from: https://www.mdpi.com/1648-9144/59/7/1296

38. Cotrim C, Palinkas ED, Cotrim N. The importance of left ventricular outflow tract and midventricular gradients in stress echocardiography: a narrative review. *J Clin Med*. 2023;12(16):5292.

39. Liguori G, Feito Y, Fountaine C, Roy B, American College of Sports Medicine. *ACSM's Guidelines for Exercise Testing and Prescription - American College of Sports Medicine*. eleventh ed. PA: Lippincott Williams & Wilkins; 2021.

40. U.S. Department of Health and Human Services. *Physical Activity Guidelines for Americans*. second ed. Washington, DC: US: Department of Health and Human Services; 2018.

41. Centers for Disease Control and Prevention. *Perceived exertion (Borg rating of perceived exertion scale)*. 2022. 2022 [cited 2024 Apr 13]. Available from: https://www.cdc.gov/physicalactivity/basics/measuring/exertion.htm

42. World Health Organization. *WHO guidelines on physical activity and sedentary behaviour*. 2020. 2020 [cited 2023 Sep 29]. Available from: https://www.who.int/publications/i/item/9789240015128

43. Gati S, Sharma S. Exercise prescription in individuals with hypertrophic cardiomyopathy: what clinicians need to know. *Heart*. 2022;108(24):1930.

44. Emery MS, Martinez MW. HCM exercise prescription. 2023. *Am College Cardiol*. 2023 [cited 2024 Apr 12]. Available from: https://acc.bravais.com/s/1IBRL3FX5SOCaEcrFbxB

45. Pelliccia A, Sharma S, Gati S, et al. 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease: the Task Force on sports cardiology and exercise in patients with cardiovascular disease of the European Society of Cardiology (ESC). *Eur Heart J*. 2021;42(1):17–96.

46. Kiuchi M, Schlaich M, Ho J, Carnagarin R, Villacorta H. *Lifestyle advice for patients with ICDs: physical activity - what is healthy and what is contraindicated*. 2019. 2019 [cited 2024 Apr 13];17:Online. Available from: https://www.escardio.org/Journals/E-Journal-of-Cardiology-Practice/Volume-17/lifestyle-advice-for-patients-with-icds-physical-activity-what-is-healthy-and-what-is-contraindicated

47. Saarel E, Law I, Berul C, et al. Safety of sports for young patients with implantable cardioverter-defibrillators: long-term results of the multinational ICD sports registry. *Circ Arrhythm Electrophysiol*. 2018;11:e006305.

48. Pelliccia A, Solberg EE, Papadakis M, et al. Recommendations for participation in competitive and leisure time sport in athletes with cardiomyopathies, myocarditis, and pericarditis: position statement of the Sport Cardiology Section of the European Association of Preventive Cardiology (EAPC). *Eur Heart J*. 2019;40(1):19–33.

49. Aengevaeren V, Gommans F, Dieker HJ, et al. Association between lifelong physical activity and disease characteristics in HCM. *Med Sci Sports Exerc*. 2019;51:1.

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